UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

CASWELL FILE 12

SUBJECT: Exemption from the requirements of a tolerance for Dimethylsulfoxide (DMSO), CB review of 7/24/74, R. Beyack

DATE: September 9, 1974

000177

FROM:

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

TO: Mr. Lee TerBush, Acting Chief
Coordination Branch
Registration Division (WH-567)

Pesticide Petition No. 4F1486
Related Petitions: 1E1017 & 3E1364

Crown Zelerbach Corp.
Camas, Washington

CB has deferred to TB the question of unidentified residues of DMSO in meat, eggs and milk resulting from this proposed use as a solvent or cosolvent. In our initial review of this petition (memo of 5/2/74, Dr. C. H. Williams) TB concluded that the proposal for clearance of DMSO under 180.1001(d) with a 24 hour PHI could be granted, CB considerations permitting, and that the previous proposal limiting application to "....before formation of edible parts...." was based on CB's estimate that no more 1 ppm residue of DMSO and $DMSO_2$ could be expected (review of 4/18/73, PP #3E1364, A. Rathman), and was supported by the available toxicity data.

However, Mr. Beyak has concluded:

1. Plant residues are adequately characterized and consist of 85% DMSO and $DMSO_2$.

2. Proposed use will result in pesticide residues at levels up to 2 ppm in edible portions of fruits and vegetables and at levels up to 6 ppm in grains.

3. The feeding of DMSO to animals will result in residues in meat, eggs and milk; the identification and levels of metabolites are questionable.

4. The sensitivity of the analytical method is only about 3 ppm.

Conclusions

1. TB considers that the question of unidentified residues in plants is adequately answered; we are not concerned further with such residues. Further characterization needed, however, for meat, eggs and milk residues.

2. We consider that 2 ppm residues in fruits and vegetables and 6 ppm levels in grains represents a toxicologically significant exposure of DMSO in the human dietary; accordingly we recommend that serious consideration be given to establishing tolerances for this material rather than granting the proposed exemption. USDA at one time considered that DMSO was an "active ingredient" of pesticide formulations since it could be expected to enhance significantly the activity of the economic poison with which it was to be used (memo of Policy, H. W. Hays, Director, PRD/USDA, 6/6/68). This being the case, we also recommend that consideration be given to the possibility that tolerance levels of pesticides used in conjunction with DMSO might be inadequate by virtue of increased translocation into the plant; e.g., with foliar application.

The propensity of DMSO for enhancing absorption of chemicals across the skin (see literature review of R.P. Schmidt, PP #1E1017, 12/16/71) raises questions as to user/applicator safety from the active ingredient in formulations containing DMSO which must be addressed before we can register any more of such formulations.

Recommendations

1. We recommend that the proposed exemption for DMSO in section (d) with a 24 hour PHI not be granted because of 1 and 2 above.

2. We defer to CB as to whether the use of DMSO in pesticide formulations may result in higher-than-legal residues of such pesticides and/or their metabolites in subject racs.

3. We recommend that petitioner submit a full tolerance petition for DMSO as it is to be used (including the 24 hour PHI).

4. Further characterization of the unidentified metabolites in meat, eggs and milks is needed.

5. An analytical method acceptable to CB for tolerances enforcement purposes is needed.

9/9/74

David L. Ritter, Pharmacologist
Toxicology Branch
Registration Division (WH-567)

cc: CB Div. File PP No. 4F1486 Init: CHWilliams
EEB Br. File DLRitter/ccw 9/9/74

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

CASWELL FILE

October 17, 1974

pc 000177

MEMORANDUM OF A CONFERENCE

Present: Dr. J. McCarthy) FMC Corp.
R. Hawk)

Dr. Knoll) Celamerck (West Germany)
Dr. Eichler)

J. Shaughnessy) CB
W. Cox)

Dr. G. Whitmore) TB
D. Ritter)

Charlotte Young) COB

Subject:

Inerts clearance for [redacted] and [redacted] to be used in formulations containing triforine, a systemic fungicide which is to be used on apples (not registered yet).

Visitors discussed residue data in apples obtained in Germany and in USA. [redacted] residues in Germany were 0.2 - 0.3 ppm and in USA residues of [redacted] were on the order of 0.1 - 0.15 ppm (reflecting slightly lower application rates. Data were obtained the day after application. (Day "0").

For [redacted] the values from Germany were 0.3 ppm at day 0 and there were no detectable residues from USA data, i.e., less than 0.15 ppm [redacted]

Visitors wanted to know what toxicity data they would need beyond that already available from DuPont (PP #1F1026) for [redacted] and what data they would need for [redacted] Dr. Whitmore said that we should have dog and rat 90-day feeding studies for (d) but that additional data would depend on residues likely to appear in the racs and this would be decided by CB.

Dr. McCarthy then mentioned that somewhere along the line in talking to FDA it was decided that 0.5 ppm or more residues would require long-term feeding studies and did we have any feelings about this? We replied that we were in a gray area and not had to seriously consider such a requirement before.

Inert ingredient information may be entitled to confidential treatment

I then mentioned that if they had substantial amounts of data on their inerts, they should consider going the petition route for an exemption, not only because of the data but also because there may be a question of real residues.

Mr. Hawk asked about clearance for [redacted] saying that it is only one methyl group removed from [redacted] which is cleared under (c). I replied that he merely write a letter asking that we consider this for addition to 180.1001 and cite any toxicity bibliography which he might have, as well as any previous clearances under 121.

David Ritter 10/25/74

David L. Ritter, Pharmacologist
Toxicology Branch
Registration Division (WH-567)

cc:
Div. File
Br. File

DLRitter/ccw
10/25/74

Inert ingredient information may be entitled to confidential treatment

February 11, 1974

Meeting on DMSO reveals studies of old 'wonder drug' are resuming

Even its most enthusiastic promoters concede that dimethyl sulfoxide (DMSO), the drug that slips through the dermal barrier with remarkable ease, was probably discovered and used too soon.

If it had come along later, when standards for clinical trials were a little more strict, perhaps it would have fared better.

Perhaps.

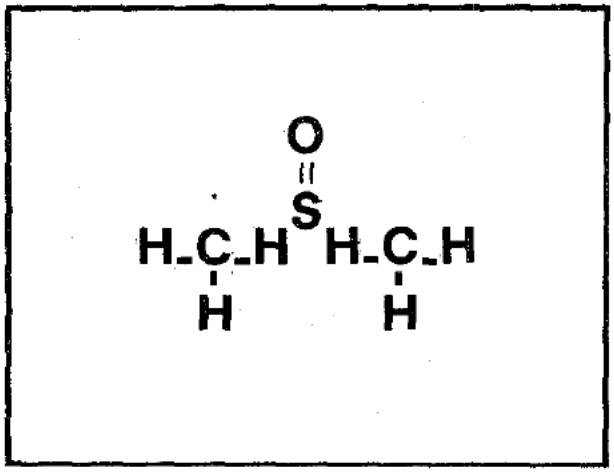
Partly, it was a case of bad luck. Somewhere back there in the 1960s, there came to be too much talk about this "wonder drug"—and too little carefully controlled experimentation. At one point, a single pharmaceutical company had the drug in the hands of 553 clinical investigators; more than 100,000 patients are estimated to have received DMSO in 1964 and 1965. Word got out, and people began rubbing the industrial grade of DMSO (also used as a solvent of paints and plastics) on their skin for a variety of ailments.

The Food and Drug Administration clamped down on clinical testing (some say too harshly). The agency cited reports of refractive changes in the eyes of experimental animals as its reason. Pharmaceutical firms lost interest in financing research, and many investigators shied away from the controversial drug.

Today, however, DMSO seems to be making something of a comeback, as indicated by a recent conference sponsored by the New York Academy of Sciences. The meeting featured a variety of encouraging reports from this country, The United Kingdom, and South America on the drug's clinical applications and potential for future use.

From South America, where extensive clinical testing has proceeded under less-strict controls, there were several reports of DMSO's efficacy in conditions ranging from carcinoma to mental retardation. While the South American investigators who reported at the New York meeting are highly respected medical specialists, some of their studies met the same criticism that doomed many United States studies of a decade ago: the lack of proper controls.

Noteworthy American studies included a report from Chicago on improvement in dogs treated with DMSO after spinal cord injuries, and a preliminary report from the University of Oregon, offering some hope that mental retardation might be somewhat improved by giving children oral doses of DMSO.



Barbara Bateman, PhD, and co-workers Michael Dunn, MD; Jeanne Gabouri, and Stanley Jacob, MD, stress that, while DMSO-treated children showed some improvement in behavior and performance, their one-year study is not complete, and is continuing into a second year. (A discouraging aspect of giving DMSO orally is that this has been associated with liver toxicity. The latest report on this comes from a study of Argentinian prisoners.)

The New York meeting was held shortly after the release of the report of a committee of the National Academy of Sciences-National Research Council, formed to advise FDA on DMSO. In general, the report urges FDA to stick to its policy of strictly limiting clinical testing. Further studies were urged, however, particularly of DMSO's efficacy in treating conditions of the musculoskeletal system, interstitial cystitis, certain mental conditions and scleroderma, and as a potential vehicle for other therapeutic agents.

The NAS-NRC committee concluded that "therapeutic effects in a significant number of patients might be anticipated" when the drug is used to treat musculoskeletal conditions.

continued on next page

TOXICOLOGY AND APPLIED PHARMACOLOGY 29, 340–347 (1974)

A Comparative Study of the Influence of Dimethyl Sulfoxide on Iodine Metabolism in Male Long-Evans Rats and Male CF_1 Mice

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Received August 16, 1973; accepted March 5, 1974

A Comparative Study of the Influence of Dimethyl Sulfoxide on Iodine Metabolism in Male Long-Evans Rats and Male CF_1 Mice. GOLDMAN, M. AND GRAU, T. J. (1974). *Toxicol. Appl. Pharmacol.* **29**, 340–347. Young adult, male, Long-Evans rats 60–70 days of age, and young adult, male CF_1 mice, 90–100 days of age were injected with 85% dimethyl sulfoxide (DMSO). Several indices of thyroid function were examined in both mice and rats: iodide transport (T/S ratio), the response of the thyroid gland to injection of an acute substantial iodide load such as organification of the trapped iodide, and thyroidal ^{131}I uptake as a function of time both *in vivo* and *in vitro*. There was no significant difference between saline-injected and DMSO-injected groups in thyroid:serum radioiodide concentration ratios (T/S) in either rats or mice. The injection of 200 μg carrier iodide elicited the acute Wolff-Chaikoff block in thyroid hormone synthesis in rats and mice and was not influenced by prior injection of 85% DMSO. Chromatographic analyses of thyroid Pronase hydrolysates in saline-injected and DMSO-injected groups of rats and mice revealed a pattern of distribution in thyroid labeling which was similar: a marked reduction in the percentage of labeled iodotyrosines and iodothyronines, an increased percentage of ^{131}I-labeled iodide, and elevated monoiodotyrosine:diiodotyrosine ratios. DMSO did not influence thyroidal ^{131}I uptake either in mice or rats. These findings indicate that 85% DMSO did not exert any significant influence on thyroid function either in the rat or mouse.

Dimethyl sulfoxide (DMSO) is an organic substance of low toxicity that has many biological activities such as dermal penetrant action (Kligman, 1965; Brown *et al.*, 1963), bacteriostatic action (Seibert *et al.*, 1967), radioprotective action (Ashwood-Smith, 1967) and anti-inflammatory action (Teigland and Saurino, 1967). Hagemann and Evans (1968) have reported that DMSO depressed ^{131}I uptake by mouse thyroid gland both *in vivo* and *in vitro* and suggested that DMSO inhibited thyroid function. However, a recent report indicates that DMSO failed to alter thyroid function in the Sprague-Dawley rat (Goldman, 1973). While Smith *et al.* (1967) have reported a lack of species variation in response to DMSO activity, species differences in regard to thyroid function among rats and mice have been reported (Wollman and Reed, 1959; Silverstein and Bates, 1961). Accordingly, an investigation into the comparative aspects of DMSO influence on thyroid activity in rats and mice was deemed necessary and so a parallel study of DMSO activity on CF_1 mice and Long-Evans rats was initiated.

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METHODS

Male Long-Evans rats (*Rattus norvegicus*) 213 ± 9 g, 60–70 days of age, and male CF_1 mice (*Mus musculus*) 34.8 ± 1 g, 90–100 days of age, were used in this study. Both the rats and the mice were maintained on Purina Laboratory chow and water ad libitum.

DMSO[1] was initially used at 2 different doses, 63% and 85% (v/v in physiological saline), but the lower dose was discontinued when no significant changes were found with that dose. All control rats were injected ip with 0.5 ml physiological saline, and control mice were injected ip with 0.25 ml physiological saline.

The methods used for the thyroid:serum radioiodide concentration ratio (T/S), the distribution of ^{131}I in unhydrolyzed and hydrolyzed thyroid glands in rats, were essentially the same as those described by Goldman (1973).

Thyroid:Serum Radioiodine Concentration Ratio (T/S)

The mice were injected ip with 2.5 mg methimazole[2] in physiological saline in order to block organification of iodine, followed 1 hr later by an injection of 3–5 μCi of carrier-free ^{131}I.[3] The administration of the radioiodine was preceded by a single ip injection of 0.25 ml DMSO in a concentration of 63% or 85% 5 min before the injection of the ^{131}I. One hour later the animals were anesthetized with ether. Blood was obtained from the dorsal aorta immediately preceding removal of the thyroid glands, and an aliquot of serum counted in a Nuclear-Chicago well-type scintillation counter in order to determine the radioactivity in 1 ml of serum. The thyroid glands were rapidly dissected, carefully weighed, and homogenized in 0.3 ml of NaCl·Tris buffer, pH 8.5, in a small, glass, motor-driven homogenizer and an aliquot of homogenate was counted to determine the amount of radioactivity in 1 g of thyroid tissue. The T/S ratio was calculated by determining the ratio of radioiodide per gram of thyroid to that of the radioiodide per milliliter of serum (Rosenberg *et al.*, 1964).

Distribution of ^{131}I in Hydrolyzed Thyroid Glands

Mice (90–100 days of age) received 0.25 ml of 85% DMSO ip, which was followed 5 min later by an injection of 20 μCi ^{131}I together with 200 μg carrier iodide. The thyroid glands were removed 1 hr later, homogenized immediately in 0.3 ml NaCl-Tris buffer, pH 8.5, and hydrolyzed with Pronase.[4] The radioiodine uptake was determined by counting the radioactivity in an aliquot of homogenate. Paper chromatography was used to fractionate the iodinated amino acids of the hydrolyzate in a collidine–3 N ammonia (3:1 v/v) solvent system for 16 hr. Autoradiography located the position of the bands containing the labeled iodinated amino acids on the chromatograms. These bands were then cut out and placed in glass vials; the radioactivity was determined according to the procedure of Rosenberg *et al.* (1964).

[1] Obtained from Mallinckrodt, St. Louis, Missouri.
[2] 1-Methyl-2-mercaptoimidazole, donated by Eli Lilly and Company, Indianapolis, Indiana.
[3] Obtained from New England Nuclear, Boston, Massachusetts.
[4] *Streptomyces griseus* protease, Calbiochem, Los Angeles, California.

Distribution of ^{131}I in Unhydrolyzed Thyroid Glands

Mice were injected ip with 85% DMSO followed 5 min later by an injection of 20 μCi ^{131}I together with 200 μg iodide. The thyroid glands were dissected and homogenized in a NaCl-Tris buffer, pH 8.5 and substantial aliquots of the unhydrolyzed glands were chromatographed using the same solvent system as above. Autoradiographs of the chromatograms localized the radioactivity into 2 bands: a band at the origin assumed to represent organic iodine, and a band of iodide. The concentration of newly formed protein bound iodine (PB^{127}I) and iodide ^{127}I were calculated from the specific activity of the injected iodide, ^{131}I uptake, and the fraction of ^{131}I at the origin according to the procedure of Rosenfeld and Rosenberg (1966).

Thyroidal ^{131}I Uptake

Thyroidal radioiodine uptake in rats was determined by 2 different methods:

In vitro method. Rats received an injection ip of 0.5 ml 85% DMSO or saline, which was followed 5 min later by an injection of 2 μCi ^{131}I. The thyroid glands were removed 1 hr later, placed in 1 ml Bouin's solution, and the uptake of the injected ^{131}I by the gland expressed in terms of the percentage of the injected dose.

In vivo method. Rats received an injection ip of 0.5 ml 85% DMSO or saline, followed 5 min later by an injection of 5 μCi ^{131}I, and the thyroidal ^{131}I uptake measured at 1, 4, and 7 hr after the injection of the radioiodine by external neck counts taken over the thyroid region, following the procedure described by Goldman (1973).

Thyroidal radioiodine uptake in mice was determined *in vitro*: Mice received an injection ip of 0.25 ml 85% DMSO or saline followed 5 min later by an injection of 2 μCi ^{131}I. The thyroid glands were removed 1 hr later and the ^{131}I uptake determined as in the procedure followed for the rats.

Values are expressed as the mean ± SE, and statistical comparisons were based on Student's t test; a p value <0.01 was considered statistically significant.

RESULTS

Thyroid: Serum Radioiodide Concentration Ratio (T/S)

Table 1 summarizes the data obtained of the effects of DMSO on the thyroid: serum radioiodide concentration ratio (T/S) in CF_1 mice and Long-Evans rats. Neither 63% DMSO nor 85% DMSO affected the thyroid ability to trap iodide as evidenced by the T/S ratios which were not significantly different in DMSO-injected, saline-injected and nontreated mice and rats. The T/S values for the saline control and noninjected control mice and rats are typical of animals for that age group in our colony.

Thyroidal Organification of Iodide

Organification of thyroidal radioiodine occurs rapidly in the thyroid glands of intact mice and rats. In our colony, approximately 90% of the total radioiodine is found in the organified components of thyroid protein 1 hr after injection of ^{131}I. However, administration of an iodide load of 200 μg iodide markedly reduced the fraction of thyroidal ^{131}I organified in both mice and rats whether injected with 85% DMSO or saline (Tables 2 and 3). Although a significant increase in the fraction of organically bound ^{131}I in mice was noted, it is relatively unimportant to the marked reduction in organic iodination elicited in response to the injected iodide.

TABLE 1

EFFECT OF DMSO ON ITS IODIDE RATIO IN MALE CF$_1$ MICE AND MALE LONG-EVANS RATS[a]

Species	Treatment	No. of animals	Body weight (g)	Thyroid weight (mg)	T/S
Mouse	Untreated control	7	35.3 ± 0.4[b]	2.1 ± 0.1[b]	31.8 ± 2.2[b]
Mouse	Saline-injected	12	34.8 ± 0.8	2.3 ± 0.4	34.6 ± 3.1
Mouse	DMSO (63%)	9	32.3 ± 0.8	1.9 ± 0.2	30.2 ± 3.9
Mouse	DMSO (85%)	9	35.0 ± 0.7	1.5 ± 0.2	31.6 ± 5.2
Rat	Untreated control	10	204 ± 6.1	12.3 ± 2.0	24.2 ± 1.6
Rat	Saline-injected	15	199 ± 10.0	13.8 ± 1.3	25.8 ± 2.5
Rat	DMSO (85%)	10	213 ± 8.7	13.2 ± 1.0	21.7 ± 1.4

[a] Mice and rats received a single ip injection of either 0.25 ml DMSO (63% or 85%) or 0.5 ml 85% DMSO, respectively, 5 min before ip injection of ^{131}I; thyroid glands were removed 1 hr later and thyroid radioiodide concentration:serum radioiodide concentration ratio was calculated.

[b] Mean value ± SE.

TABLE 2

EFFECT OF DMSO ON ORGANIFICATION OF AN INJECTED IODIDE LOAD IN MALE CF$_1$ MICE 90 DAYS OLD AND MALE LONG-EVANS RATS 60 DAYS OLD[a]

Species	Treatment	Animals	^{131}I uptake, (%) injected dose/mg	^{131}I organically bound	Organic iodine newly formed (ng/mg)	Inorganic iodide accumulated (ng/mg)
Mouse	Control	8	0.07 ± 0.0[b]	2.5 ± 1.4[b]	2.5 ± 1.0[b]	130.3 ± 12.3[b]
Mouse	DMSO (85%)	8	0.06 ± 0.0	6.1 ± 1.4[c]	7.7 ± 1.4[c]	117.3 ± 14.0
Rat	Control	8	0.02 ± 0.0	11.8 ± 1.9	2.6 ± 0.4	22.6 ± 1.9
Rat	DMSO (85%)	8	0.02 ± 0.0	10.1 ± 2.1	2.1 ± 0.5	27.6 ± 2.7

[a] Mice and rats received a single ip injection of either 0.25 ml or 0.5 ml 85% DMSO, respectively, 5 min before ip injection of 20 μCi ^{131}I plus 200 μg carrier iodide; thyroid glands were removed 1 hr later, homogenized, and chromatographed.

[b] Mean value ± SE.

[c] $p < 0.01$.

Radioiodine Distribution in Components of Pronase Thyroid Hydrolyzates

Chromatographic analyses of thyroid hydrolyzates of mice and rats showing the distribution of iodinated compounds are shown in Table 3. A severe depression in percentage of thyroidal labeled iodothyronines ($T_3 + T_4$) and iodotyrosines (MIT and DIT) occurred in saline-injected and 85% DMSO-injected mice and rats that had been iodide-loaded. The large increase in the fraction of labeled iodide occurred both in saline-injected and 85% DMSO-injected mice and rats and there was no significant difference in percentage of thyroidal label in this component. These results are consistent with the data observed in Table 2 showing the marked impairment in thyroidal capacity to bind iodine organically after injection of 200 μg iodide.

The fraction of thyroidal label in MIT is considerably higher than in DIT in mice and rats whether injected with saline or 85% DMSO due to the injection of 200 μg iodide and results in a significant increase in MIT/DIT ratio compared with untreated mice and rats not receiving an iodide load (Table 3).

TABLE 4

EFFECT OF DMSO ON ^{131}I UPTAKE 1 HR AFTER INJECTION IN MALE CF$_1$ STRAIN MICE 90–100 DAYS OF AGE AND IN MALE LONG-EVANS RATS 60–70 DAYS OF AGE (*in Vitro*)[a]

Species	Treatment	No. of animals	^{131}I Uptake (% injected dose)
Mouse	Control	6	1.01 ± 0.19[b]
Mouse	DMSO (85%)	8	0.99 ± 0.11
Rat	Control	5	1.80 ± 0.21
Rat	DMSO (85%)	5	1.59 ± 0.29

[a] Mice and rats received a single ip injection of either 0.25 ml or 0.5 ml of 85% MDSO, respectively, 5 min before ip injection of radioiodine; thyroid glands were removed 1 hr later, placed in counting vials, and percent ^{131}I uptake was calculated.

[b] Mean value ± SE.

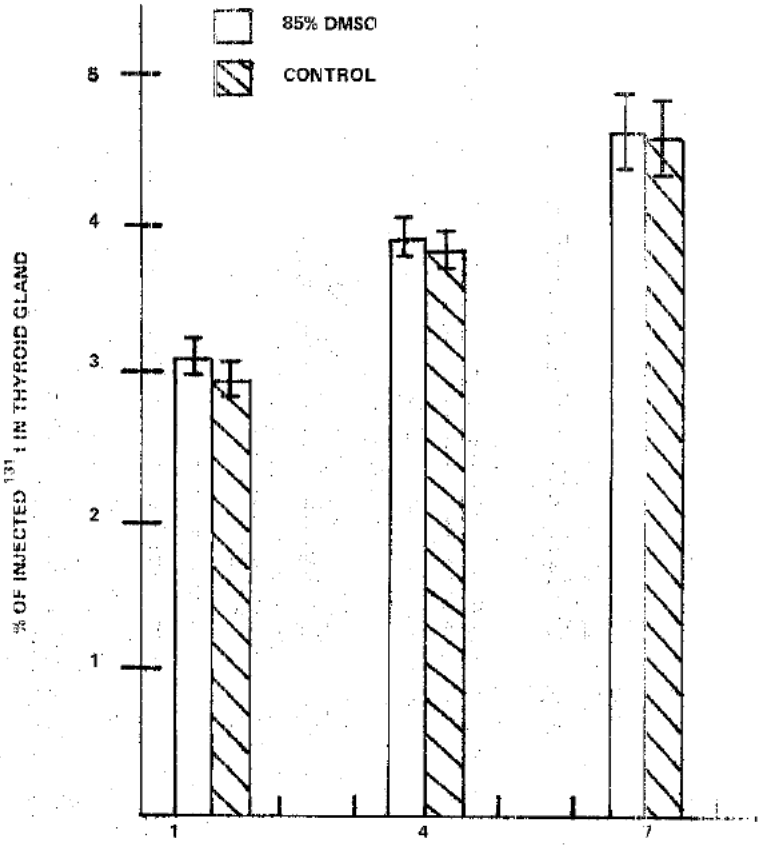

FIG. 1. The effect of 85% DMSO on thyroidal ^{131}I uptake in rats (*in vivo*). Rats received ip injection of 0.5 ml 85% DMSO 5 min before ip injection of ^{131}I; neck counts were taken 1, 4, and 7 hr after radioiodine administration, and the percent ^{131}I uptake was calculated. Vertical lines represent ±SE. There were 7 rats in the control group and 8 rats in the 85% DMSO-injected group.

Inhibition of iodothyronine synthesis, Wolff-Chaikoff effect (Wolff and Chaikoff, 1948; Wolff *et al.*, 1949), due to iodide block in organification of iodine was not affected in mice and rats by prior injection of saline or 85% DMSO.

Thyroidal Radioiodine Uptake

In vitro studies. The effect of 85% DMSO on the thyroidal uptake of ^{131}I 1 hr after injection of the radioiodine is shown in Table 4 for mice and rats. There was no significant difference in radioiodine uptake observed in mice and rats whether injected with saline or 85% DMSO.

In vivo studies. Figure 1 shows the effect of 85% DMSO on the thyroidal uptake of ^{131}I at 1, 4 and 7 hr after injection with radioiodine. There was no significant difference in radioiodine uptake at any time between the saline-injected and 85% DMSO-injected rats.

DISCUSSION

In view of the conflicting results obtained by Hagemann and Evans (1968) in the mouse and by Goldman (1973) in the rat as to whether DMSO influences thyroid function, the present investigation was initiated as a comparative study of the effect of DMSO on thyroid function in the Long-Evans rat and CF_1 mouse.

The results of this study do not demonstrate that DMSO was significantly effective in depressing the active transport of iodide in either the Long-Evans rat or the CF_1 mouse and are therefore at variance with the suggestion of Hagemann and Evans (1968) that DMSO inhibits this phase of thyroid function (Table 1). The data do confirm the previous findings in this laboratory of the failure of either 63% or 85% DMSO to inhibit iodide transport in the Sprague-Dawley rat (Goldman, 1973).

The acute response to a single large iodide load by the thyroid gland results in both quantitative and qualitative changes in thyroid hormone synthesis due to decreased organic binding of iodide (Galton and Pitt-Rivers, 1959). This temporary inhibition in organification of iodide as a consequence of large doses of iodide is known as the Wolff-Chaikoff effect and is dependent upon the accumulation of a critical concentration of iodide within the thyroid gland (Raben, 1949). Evaluation of the thyroidal accumulation of organic iodine newly formed after administration of an iodide load (Deodhar and Rosenberg, 1969) may therefore offer a convenient means of assessing the gland's ability for hormone synthesis. The results reported here do not confirm Hagemann and Evans' (1968) suggestion that DMSO inhibits thyroidal organification of iodide either in mice or rats (Table 2). There was no evidence of an inhibitory action of DMSO on thyroid hormone synthesis beyond that induced by the antithyroid action of excess iodide itself.

The pattern of distribution in thyroid labeling showed a marked diminution in the percentage of labeled iodotyrosines and iodothyronines with an increased percentage of ^{131}I-labeled iodide in both rats and mice whether injected with saline or DMSO (Table 3). The high MIT/DIT ratios observed in both rats and mice reflected the increased proportion of labeled MIT relative to DIT which occurs when organification of iodine is severely deficient (Galton and Pitt-Rivers, 1959).

The inhibitory effect of DMSO on thyroidal uptake of ^{131}I in mice reported by Hagemann and Evans (1968) could not be confirmed in this investigation in CF_1 mice.

More ... radioiodine uptake by DMSO was observable in Long-...

The ... DMSO does not have a significant effect on thyroid activity ... rats or male CF_1 mice. While data reported herein do not ... inhibitory action of DMSO on thyroid function in the mouse ... Evans (1968), they do confirm the findings of Goldman ... DMSO failed to influence any of the parameters of thyroid ... the Sprague-Dawley rat.

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R034487

Chemical:	**Dimethyl sulfoxide**
PC Code:	**000177**
HED File Code	**11000 Chemistry Reviews**
Memo Date:	**09/09/74 12:00:00 AM**
File ID:	**00000000**
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